

Immunogenicity of a booster dose of a typhoid conjugate vaccine (TCV) in Malawian pre-school children.

Nginache Nampota-Nkomba^{1,2}, Oswald M Nyirenda¹, Shrimati Datta², Victoria Mapemba¹, Priyanka D Patel³, Theresa Misiri³, Felistas Mwakiseghile³, John M Ndaferankhande³, Bright Lipenga³, Jennifer Oshinsky², Marcela F Pasetti², Leslie P Jamka², Melita A Gordon^{3,4}, Matthew B Laurens², Kathleen M Neuzil^{2,5}

Introduction

- A phase 3 trial of Vi polysaccharide-tetanus toxoid (Vi-TT) conjugate vaccine in Malawi, randomized children 1:1 to Vi-TT or meningococcal A polysaccharide tetanus toxoid (Men-A) conjugate vaccine
- Single dose Vi-TT was 78.3% efficacious against typhoid fever for 4+ years
- Compared to older children, children vaccinated <2 years old had:
 - Modestly lower efficacy (70.6%) at 4 years post-vaccination
 - Quicker waning of anti-Vi immunoglobulin G (IgG) at 2 years post-vaccination

Objectives:

- Persistence of typhoid immunity conferred by Vi-TT at 4 years post-vaccination
- Immunogenicity of booster dose of Vi-TT given at 5 years of age

Methods

Study design: Open label clinical trial of children vaccinated at 9-11 months old (n=136)

Study population:

- Booster-TCV:** Vi-TT booster dose at 5 years (n=72)
- 1st-TCV:** First Vi-TT dose at 5 years (n=64)

Study procedures:

- Serum collection: days 0, 28, and 160-180 post-vaccination
- Tests: anti-Vi IgG and IgA, and anti-tetanus IgG by ELISA
- Seroconversion (Vi-TT): ≥ 4 -fold rise in anti-Vi from day 0 to days 160-180 post-vaccination
- Seroprotection (tetanus): Anti-tetanus IgG ≥ 0.1 IU/mL (short-term) and ≥ 1.0 IU/mL (long-term) at day 28 and day 160-180 post-vaccination

Results

Anti-Vi IgG immunogenicity

- Anti-Vi declined 4 years post-vaccination
 - Higher levels in children who received Vi-TT at 9-11 months old
- Booster Vi-TT at 5 years produced a robust immune response
 - Higher than initial response at 9-11 months
 - Higher than a first vaccination at 5 years
- Similar results for IgA response

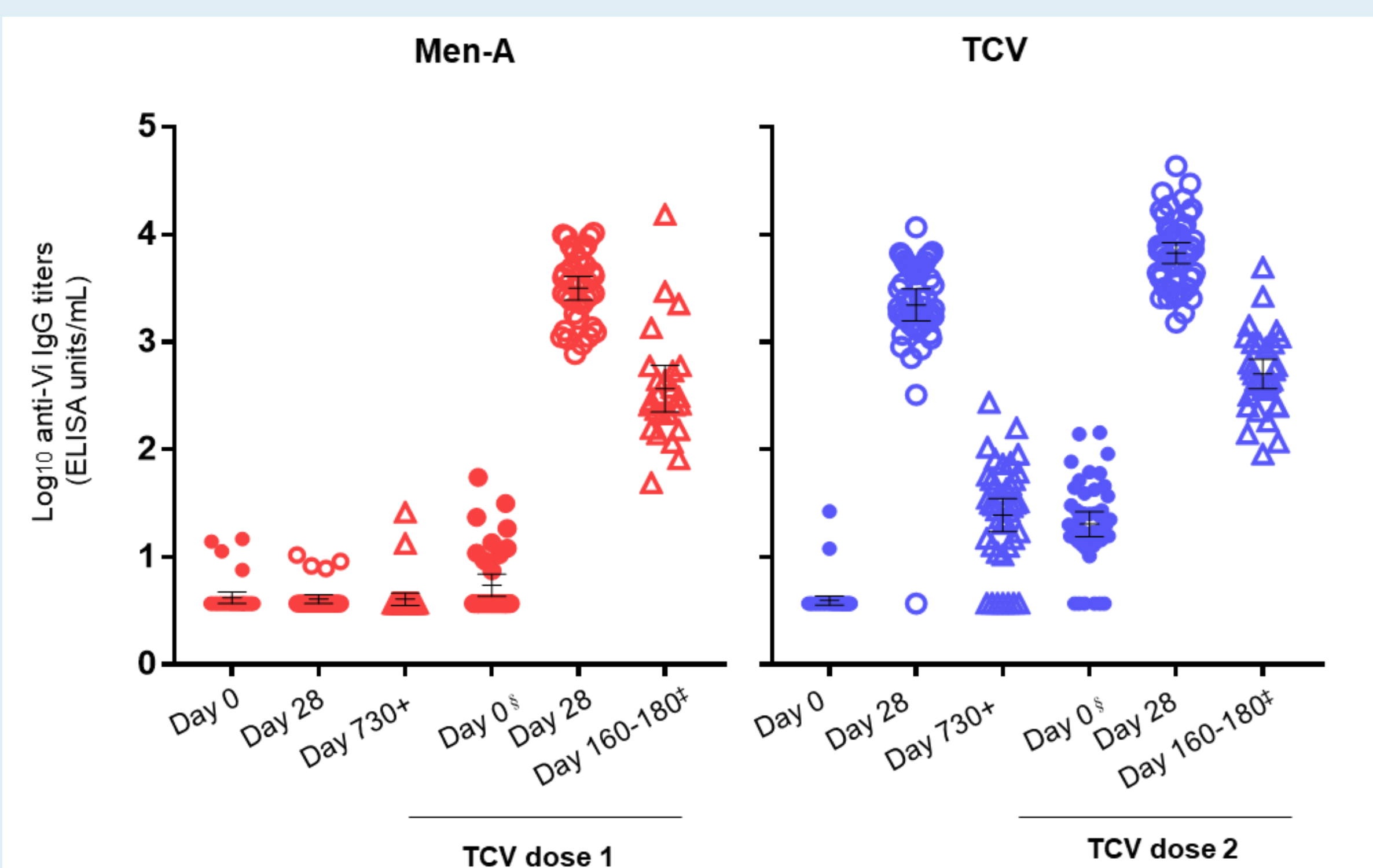


Figure 1. Anti-Vi IgG before and after first Men-A or Vi-TT vaccination and before and after Vi-TT vaccination given 4 years after receipt of first Vi-TT or Men-A

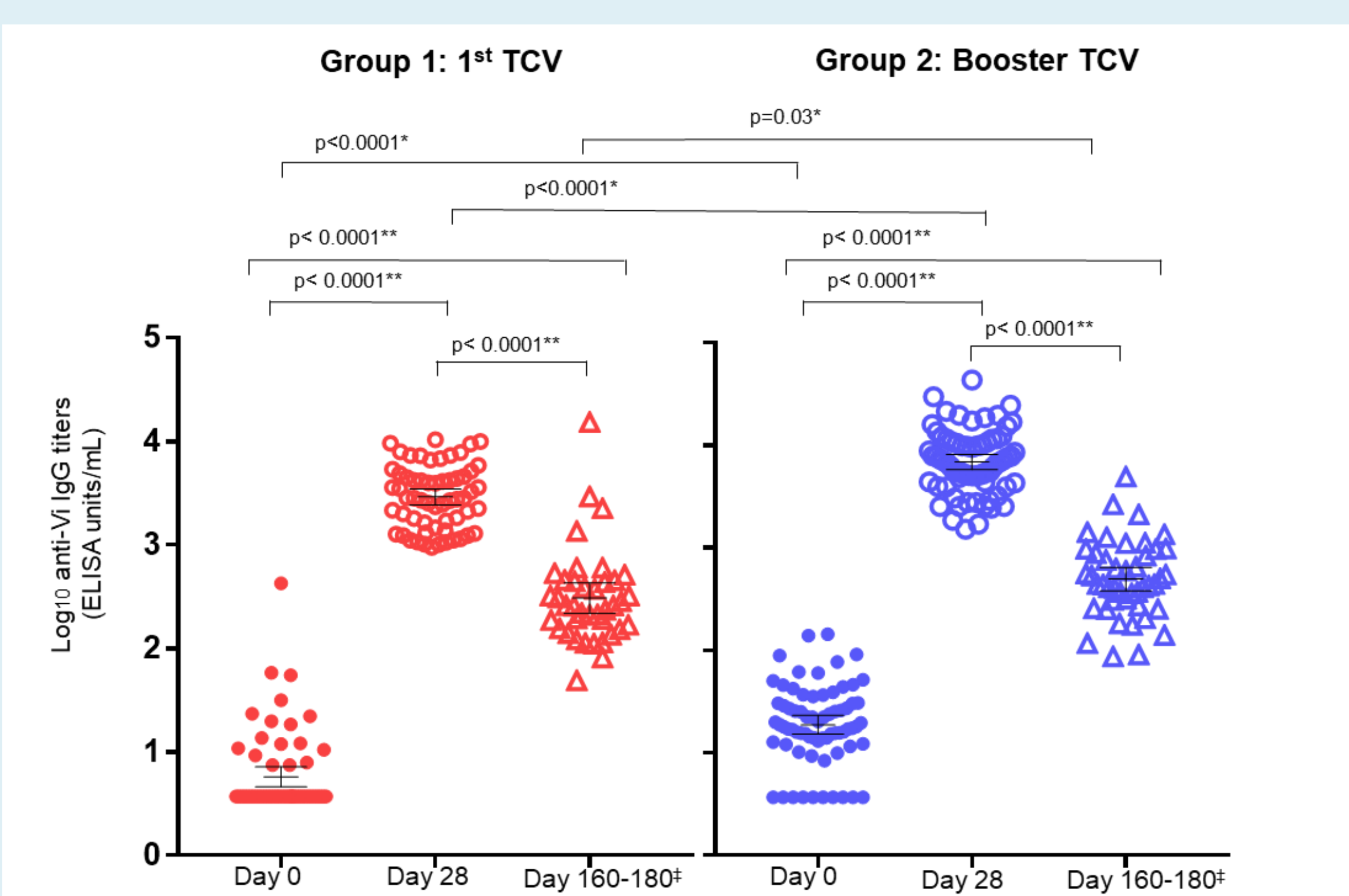


Figure 2. Anti-Vi IgG GMT before, 28 and 160-180 days after Vi-TT vaccination given 4+ years after receipt of first Vi-TT or Men-A

Table 1. Anti-Vi IgG before, 28 and 160-180 days after Vi-TT vaccination

	Booster-TCV		1st-TCV	
	n or n/N	Mean or % (95% CI)	n or n/N	Mean or % (95% CI)
GMT (Elisa Units/mL)				
Day 0	71	19 (15-23)	64	6 (5-7)
Day 28	70	6868 (5794-8141)	60	2912 (2429-3491)
Day 160-180	44	495 (381-643)	39	307 (219-431)
Geometric Mean Fold Rise				
Day 0 to 28	69	376 (293-481)	60	493 (364-666)
Day 0 to 160-180	43	25 (19-34)	39	54 (38-79)
Seroconversion ≥ 4 -fold increase from				
Day 0 to 28	69/69	100 (95-100)	59/60	98 (91-100)
Day 0 to 160-180	41/43	95 (84-99)	39/39	100 (91-100)

Anti-tetanus IgG immunogenicity

- Vi-TT boosted anti-tetanus immunity

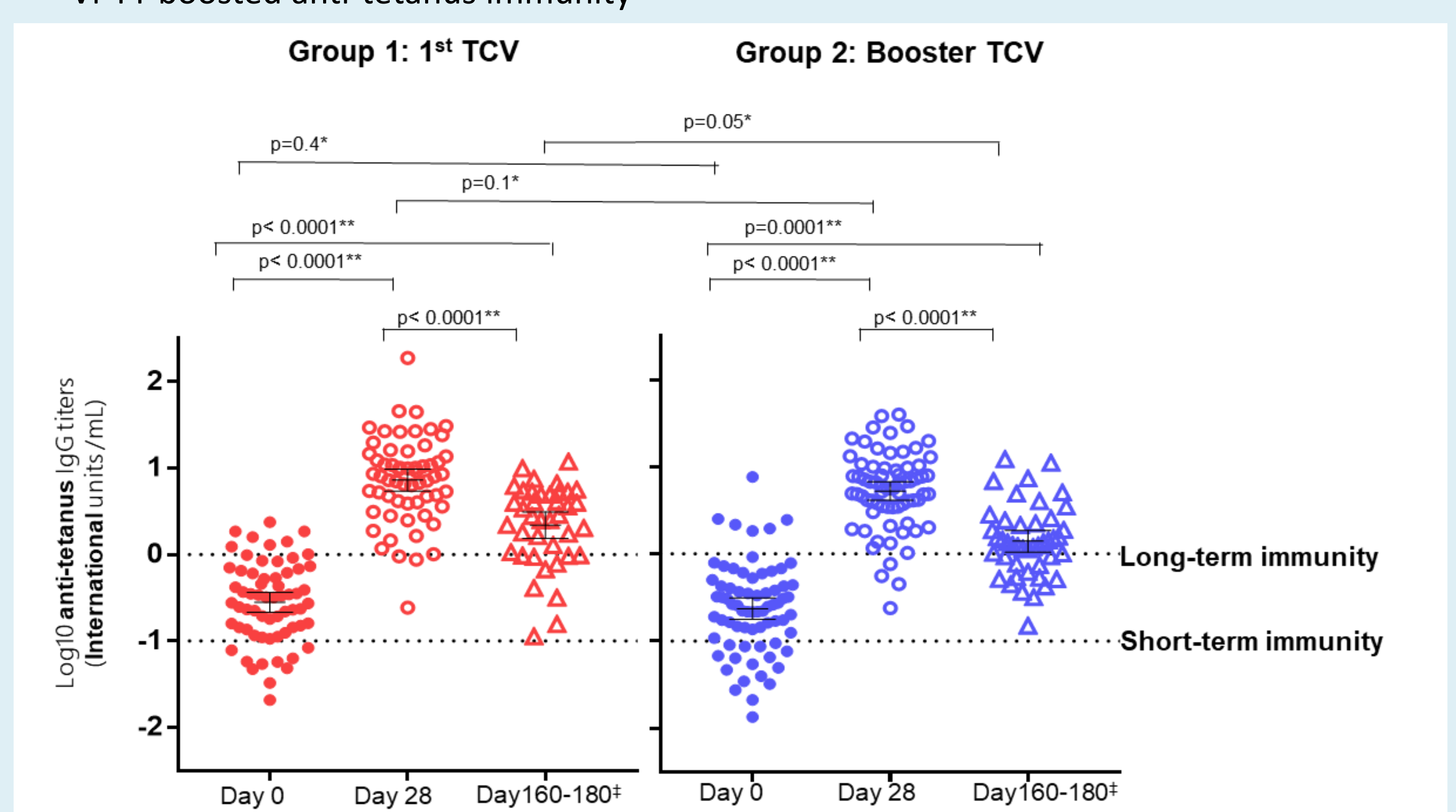


Figure 3. Anti-tetanus IgG GMT before, 28, and 160-180 days after Vi-TT vaccination given 4+ years after receipt of first Vi-TT or Men-A in the per-protocol population.

Discussion

- A Vi-TT booster at 4 years post-primary vaccination at 9-11 months elicits a robust immune response and boosts tetanus immunity
- These findings are valuable for policymakers at the global and national levels